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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/092,934	03/08/2002	Paul Averback	018792-0199	7362

22428 7590 02/22/2007
FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
SANG, HONG	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/092,934	AVERBACK, PAUL	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,20,23-38,43 and 46-54* is/are pending in the application.

4a) Of the above claim(s) *8,10-16,30,32-38,46, 52 and 53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,20,23-29,31,43,47,49-51 and 54* is/are rejected.

7)☒ Claim(s) *48* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Exhibit A*.

DETAILED ACTION

RE: Averback

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/19/2006 has been entered.

2. Clams 1-16, 20, 23-38, 43, and 46-54 are pending. New claims 52-54 are added. Claims 8, 10-16, 30, 32-38 and 46 are withdrawn from further consideration as being drawn to non-elected inventions. Claims 17-19, 21-22, 39-42 and 44-45 are cancelled. Claims 1 and 47 are amended.

3. Due to applicant's species election of SEQ ID NO.10 (see 8/23/05 response), claims 52 and 53 are withdrawn from further consideration as being drawn to non-elected inventions.

4. Claims 1-7, 9, 20, 23-29, 31, 43, 47-51 and 54 are under examination.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

6. The rejection of claims 1-7, 9, 20, 23-29, 31, 43, 47, 49-51 and new claim 54 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

a method of treating a benign tumor, a malignant tumor, hyperplasia, hypertrophy, overgrowth of a tissue and malformation of a tissue in a patient requiring removal or destruction of cells comprising locally administering (e.g. topically, intratumorally) to a mammal in need a therapeutically effective amount of the neural thread protein consisting of SEQ ID NO. 10, does not reasonably provide enablement for a method of treating any and all conditions in a patient requiring removal or destruction of cells comprising systemically administering (e.g. intravenously, intra-arterially, intraperitoneally) to a mammal in need a therapeutically effective amount of any and all neural thread protein (NTP) as well as fragments, variant, derivative, homolog, reverse-D peptide, and enantiomers of NTP is maintained.

The response states that the prior art contains detailed teachings of NTP and how to make NTP, as summarized on pages 5-6 and 9- 11 of the specification. The response states that derivatives, variants, homologs, and other forms of NTP that retain their biological activity can also be made using routine techniques well-known in the prior art, such as conservative amino acid substitutions. The response states that the specification also contains an extensive listing of conditions requiring destruction or removal of cells (see e.g., pgs. 33-34) and particular dosage forms for the NTP depending on the desired routes of administration (see e.g., pgs. 36-41). The response states that the teachings of the specification are corroborated by actual working examples, which demonstrate that NTP induced acute necrosis regardless of the type of tissues tested or its origin. The specification states that the specification teaches how to make and use examples of NTP compositions that can be administered systemically,

such as site-specific NTP compositions (pgs 34-36), for example chemotherapeutic agents can be delivered as conjugates to make the agents site specific, in addition, antibodies to NTP are known and method of making antibodies to specific targets are known in the art. The response states that there is no evidence that exposure to NTP results in instant cell death, the active site-specific NTP conjugates could be delivered to practice the claimed invention with inhibiting the activity of NTP.

Applicant's arguments have been carefully considered but are not found persuasive. Claims are drawn to a method of treating a condition in a patient requiring removal or destruction of the patient's cells comprising administering to a mammal in need a therapeutically effective amount of a neural thread protein (NTP). As indicated in the previous office action, the condition to be treated encompasses any and all conditions including normal and diseased conditions that are caused by any pathogens, genetic mutations, injuries, etc. The method encompasses *in vivo* treatment by administering to a patient a NTP either systematically or locally. A neural thread protein NTP encompasses proteins which share homology or function similarities with neuronal thread proteins either known in the art or yet to be discovered, any fragments, homologs, variants, derivatives, peptide mimetics, reverse-d peptides, and enantiomers thereof (see specification page 11, lines 10-11). The art only teaches a method of treating a benign or malignant tumor in a mammal comprising local administration of a therapeutically effective amount of a NTP-peptide selected from the group consisting of SEQ ID NOS: 23, 24, 25, 26, 28, 29, and 52 (see US Patent No. 6,924,266 B2, claims 4-7). The instant specification demonstrates that NTP induces acute necrosis

regardless of the type of tissues tested or its origin (see specification pages 45-46, Examples 2 and 3, also see response page 12, lines 15-16). The cytotoxic and necrotic effect of AD7C-NTP (SEQ ID NO. 10) is not cell selective or site selective, AD7C-NTP (SEQ ID NO. 10) is toxic to any type of cells that are in contact with it at the dose used in the specification. Neither the art nor the instant specification teach a method of treating any and all conditions in a patient requiring removal or destruction of cells comprising systemically administering to a mammal in need a therapeutically effective amount of any and all neural thread protein including AD7C-NTP (SEQ ID NO. 10), and NTP disclosed in US Patent No. 6,924,266 B2. For example, it has not been shown by the prior art or the instant specification that administering NTP to AIDs patients, the infected T cells can be selectively removed or destructed without affecting normal blood cells. It has not been shown by administering NTP systemically to bacterially infected patients, the cells that are infected by the bacteria can be selectively removed or destructed in the patients. While claim 1 has been amended to limit the cells to be patient's own cells, the patient's cell still reads on cells that are infected by bacterial or virus. Therefore, The specification has not enabled a method of treating the full scope of the condition that requiring removal or destruction of cells comprising administering any and all NTP systemically. The art and the instant specification have only enabled a method of treating tumor, hyperplasia, hypertrophy, overgrowth of tissue and malformation of tissue in a patient requiring removal or destruction of cells comprising administering locally to a mammal in need a therapeutically effective amount of certain NTPs. While specification suggests using a conjugate of NTPs, wherein the NTPs are

linked to a protein or other molecule, for *in vivo* delivery, the specification fails to teach how to make such conjugates that is tumor- or site specific and the activity of NTPs is shut down or inhibited during delivery and turned on only at required sites. As indicated in the previous office action, the NTP protein is different from chemotherapeutic drugs, which effectively target fast-dividing cells. Tumours such as leukemia and lymphoma are more sensitive to chemotherapy. The instant specification does not teach that NTP is selective to any specific type of cells. Moreover, the claims as written read on systematically delivering of a NTP that is not in conjugated form. Applicants argue that the NTP does not kill cells instantly. However, there is no data in the specification indicating the time line of NTP killing. Furthermore, the NTP encompasses fragments, homologs, variants, derivatives, peptide mimetics, reverse-d peptides, and enantiomers thereof, while the specification teaches that conservative amino acid substitutions can be made to naturally occurring NTP such that the modified NTP retains biological activity, the specification fails to provide the guidance on how to make such broad class of molecules having the same function as the NTP of SEQ ID NO.10. The specification does not teach what the structural elements are required by the genus of the NTP proteins to perform the claimed function. New claim 54 recites "a peptide at least 75% identical to SEQ ID NO.10". The specification fails to provide guidance regarding which amino acids within the full-length amino acid sequence of SEQ ID NO.10 that can be changed by deletion, addition, substitution and combination thereof such that the resulting protein is at least 75% identical to wild type protein and still has the same property as SEQ ID NO.10. Because of these reasons, it would require undue

experimentation for one skilled in the art to make and use the full scope of the NTP.

7. The rejection of claims 1-7, 9, 20, 23-29, 31, 43, 47, 49-51 and new claim 54 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained.

The response states that the specification contains an extensive description of NTPs, including a variety of specific sequences and references to scientific literature describing NTP (see e.g., pgs. 9-1 I), as discussed in detail in Applicant's May 8th amendment, for example, Figures 1-9 each list an example of a specific NTP, and an entire section is dedicated to describing the preparation of NTP, including fragments, homologs, variants, derivatives, peptide mimetics, reverse-D peptides, and enantiomers of NTP (pgs. 19-32). The specification teaches that based on this description, one of skill in the art could readily make and use different NTPs, including homologs and variants, such as by using well-known conservative amino acid substitutions. The response states that the specification does not need to provide specific examples of structural characteristics, because NTPs are a well-known class of compounds, a skilled artisan could assess structural similarity using techniques described on page 15-16 of the specification.

Applicant's arguments have been carefully considered but are not found persuasive. The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient

description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column). The specification teaches that the NTP refers to a neural thread proteins and related molecules, it also includes biologically active fragments, homologs, variants, derivatives, peptide mimetics, reverse-D peptides, and enantiomers (see page 11, lines 10-11). Although the instant specification teaches a general method for making peptide mimetics, homologs, variants, etc., it fails to provide information regarding the structures of any fragments, homologs, variants, derivatives, peptide mimetics, reverse-D peptides, and enantiomers, that is correlating with the claimed function, i.e. capable of removing or destruction of cells. The specification provides neither a representative number of fragments, homologs, variants, derivatives, peptide mimetics, reverse-D peptides, and enantiomers of nor does it provide a description of structural and functional features that are common to the fragments, homologs, variants, derivatives, peptide mimetics, reverse-D peptides, and enantiomers of the SEQ ID NO.10. Similar to other claims, new claim 54 recites "a peptide at least 75% identical to SEQ ID NO.10". There is a lack of a written description regarding which amino acids within the full-length amino acid sequence of SEQ ID NO.10 that can be changed by deletion, addition, substitution

and combination thereof such that the resulting protein is at least 75% identical to wild type protein and still has the same property as SEQ ID NO.10. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of the specific species of genus is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

8. The rejection of claims 1-7 and 9, and new claims 47, 49-51 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4-7 of U.S. Patent No. 6,924,266B2 is maintained.

The response states that the '266 patent claims a "method of treating a benign or malignant tumor in a mammal comprising local administration of a therapeutically effective amount" of one of the specifically defined NTPS recited in claim 1. The response states that based on this disclosure, one of skill in the art could not extrapolate that NTPS in general could be used to treat "a condition in a patient requiring removal or destruction of cells," as claimed. The response states that agents for the treatment of tumors do not necessarily treat all conditions requiring removal or destruction of cells.

Applicant's arguments have been carefully considered but are not found persuasive. Claims 4-7 of U.S. Patent NO. 6,924,266B2 are drawn to a method of treating a benign or malignant tumor in a patient comprising local administration of a

therapeutically effective amount of a NTP-peptide consisting of SEQ ID NOS: 23-26, 28, 29 and 52. Because the SEQ ID NOS. 23-26, 28, 29 and 52 recited in '266 patent are species of the instantly claimed genus of NTP protein, the tumor of '266 patent is a species of the genus of condition that is claimed in the instant application, and the active steps of the instant claims comprise only administering an effective amount of NTP to a mammal, therefore, claims 4-7 of U.S. Patent NO. 6,924,266B2 anticipate instant claims 1-7, 9, 47, and 49-51.

9. The provisionally rejection of claims 1-7 and 9, and new claims 47, 49-51 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-16 and 18 of copending Application No. 10/294,891 and claims 9-13 and 15 of copending Application No. 10/920,313.

The response states that applicant will address the rejection on the merits if it ever matures into a non-provisional rejection.

Applicant's response is acknowledged. Since the applicant has not taken any actions, the rejection is therefore maintained.

New Grounds of Objections

Claim Objections

10. Claims 47-51 and 54 are objected to because of the following informalities: Claim 47 contains non-elected inventions i.e. unwanted hair, and a wart. Appropriate correction is required.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1-5, 7, 9, 20, 23-27, 29, 31, 43, 47, are 49-51 rejected under 35 U.S.C. 102(e) as being anticipated by Xu et al. (US Patent No. 6,620,922B1, Date of Patent 9/16/2003, Filing Date: 8/9/2000)

Xu et al. teach a method of treating cancer such as prostate cancer comprising administering a polypeptide, including a polypeptide of SEQ ID NO. 573 (see abstract and column 2, lines 18-46, column 61, lines 55-61). Xu et al. teach that the polypeptide can be administered to a subject by oral delivery (see column 62, line 16), injectable delivery (column 63, line 15), such as intravenous, intraperitoneal, intramuscular, subcutaneous, topical (see column 72, lines 41-44), and nasal delivery (column 64, line 59). Xu et al. teach that the polypeptide can be administered in together with an immunostimulant such as cytokines GM-CSF, or interleukin-2, IL-7, or IL-12. Because the SEQ ID NO.573 is 61.5% identical to the instant claimed SEQ ID NO.10 (see sequence alignment Exhibit A), the polypeptide of SEQ ID NO.573 reads on the claimed NTP, which encompasses fragments and variants of SEQ ID NO.10. Moreover, the prostate cancer can be considered as a type of malformation of prostate.

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CHRISTOPHER H. YAEN
PRIMARY EXAMINER

Hong Sang
Art Unit 1643
Feb. 11, 2007

Exhibit A

```
<!--StartFragment-->RESULT 45
US-09-636-215-573
; Sequence 573, Application US/09636215
; Patent No. 6620922
; GENERAL INFORMATION:
;  APPLICANT:  Xu, Jiangchun
;  APPLICANT:  Dillon, Davin C.
;  APPLICANT:  Mitcham, Jennifer L.
;  APPLICANT:  Harlocker, Susan L.
;  APPLICANT:  Jiang, Yuqui
;  APPLICANT:  Henderson, Robert A.
;  APPLICANT:  Kalos, Michael D.
;  APPLICANT:  Fanger, Gary R.
;  APPLICANT:  Retter, Marc W.
;  APPLICANT:  Stolk, John A.
;  APPLICANT:  Day, Craig H.
;  APPLICANT:  Vedvick, Thomas S.
;  APPLICANT:  Carter, Darrick
;  APPLICANT:  Li, Samuel
;  APPLICANT:  Wang, Aijun
;  APPLICANT:  Skeiky, Yasir A.W.
;  APPLICANT:  Hepler, William
;  TITLE OF INVENTION:  COMPOSITIONS AND METHODS FOR THE THERAPY AND
;  TITLE OF INVENTION:  DIAGNOSIS OF PROSTATE CANCER
;  FILE REFERENCE:  210121.42717C17
;  CURRENT APPLICATION NUMBER: US/09/636,215
;  CURRENT FILING DATE:  2000-08-10
;  NUMBER OF SEQ ID NOS:  852
;  SOFTWARE:  FastSEQ for Windows Version 3.0
; SEQ ID NO 573
;   LENGTH: 132
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-09-636-215-573

  Query Match             12.3%;  Score 250;  DB 2;  Length 132;
  Best Local Similarity   61.5%;  Pred. No. 2.5e-19;
  Matches   48;  Conservative    6;  Mismatches   24;  Indels    0;  Gaps    0;

Qy        298 NFCLFEMESHSVTQAGVQWPNLGSLQPLPPGLKRFSCLSLPSSWDYGHLPPHPANFCIFI 357
              ||     ||  | |||||| :| ||||||   |:||||||| |||: : ||| |||| |
Db         27 NFFFLRQESGPVAQAGVQWHDLSSLQPLPHRFKQFSCLSLPHSWDHRYAPPHLANFCSFS 86

Qy        358 RGGVSPYLSGWSQTPDLR 375
              | |||   ||||:|| |:
Db         87 RDGVSLCCSGWSKTPGLQ 104
<!--EndFragment-->
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